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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/562,494	04/27/2006	Benjamin Oshlack	200.1163US	8290

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EXAMINER	
CLAYTOR, DEIRDRE RENEE	
ART UNIT	PAPER NUMBER
1617	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/562,494	OSHLACK ET AL.	
	Examiner	Art Unit	
	Renee Claytor	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 May 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Currently, claims 1-29 are pending and are under examination herein.

Response to Arguments

Applicants have amended claims 15-16, 18-21 and 23-26 which is sufficient to overcome the Claim Objections over claims 15-16, 18-21 and 23-26 and the 35 USC 101 and 112 rejections over claims 24-26. The rejections are hereby withdrawn.

Applicants argue over the 35 USC 103 rejection over Oshlack et al. (US PgPub 2003/0229111) that the Oshlack et al. do not describe the claimed ratio (now amended in claim 1) or suggest the desirability of the ratio.

It is noted that Oshlack et al. teaches the desirability of providing naltrexone in amounts greater than 0.001 mg and less than 20 mg as discussed in the rejection. Further, Oshlack et al. teach that hydrocodone is provided in the composition in amounts ranging between 5-20 mg. Further, Oshlack et al. teaches that in certain embodiments the composition comprises 5-20 mg hydrocodone and less than 5 mg of naltrexone. Therefore, Oshlack et al. contemplates dose ranges that fall within the ratio claimed. For example, when naltrexone is in a dose of 0.056 mg and hydrocodone is 5 mg the ratio is 0.011:1. Though Oshlack et al. does not have a specific example with the exact claimed range, Oshlack et al. teaches dose ranges that do fall within the claimed ratio. Further, because Oshlack et al. teaches dose ranges that fall within the instant claimed ranges, it would be desirable for one to optimize a dosage range between the two compositions to effectively treat pain. Accordingly, it is deemed that

the rejection is proper and a modified rejection is given below due to Applicants amendments.

Applicants argue over the 35 USC 103 rejection over Sherman et al (US 2003/0191147) in view of Kaiko et al. (2003/0031712) that the combination of the references does not teach the specific naltrexone to hydrocodone ratios as recited in claims 1 and 22.

In response to the above arguments, it is noted that Sherman et al. teach ranges of naltrexone with a minimum amount being 0.055 mg to 0.56 mg (see paragraphs 0061 and 0063). Further, Sherman teaches that the opioid agonist can be hydrocodone (paragraph 0068) in amounts of 0.1 to 300 mg (paragraphs 0071-0072). Sherman also exemplifies a composition in the claimed ratio and will be discussed in the modified rejection given below.

Claim Rejections -35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-14, 17-19, 22, 27-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Oshlack et al. (US Pg-Pub 2003/0229111).

Oshlack et al. teach pharmaceutical compositions comprised of naltrexone in amounts of no greater than 0.01 mg and less than 20 mg (paragraph 0016). Table 20A exemplifies a composition comprising naltrexone hydrochloride in an amount of 0.5 mg and hydrocodone bitartrate in an amount of 5 mg, which meets the limitation of claim 1 (paragraph 0035). Table 20A teaches a composition comprising 0.5 mg of naltrexone and 5 mg of hydrocodone, meeting the limitation of claim 2. Tables 22A, 23A, 24A, 25A, 26A and 27A exemplify a composition comprising naltrexone hydrochloride in an amount of 0.125 mg and hydrocodone bitartrate in amount of 5 mg, which meets the limitation of claims 3-5 (meeting the limitation of "about" 7.5 mg hydrocodone). It is further taught that the composition has a sustained release coat and this is accomplished with Eudragit RS30D (see Tables 9A, 10A, 11A, 12A, 13A). The examples associated with Tables 20, 22-27 all teach a process of making the compositions of the invention within the claimed ratio.

Oshlack et al. does not teach compositions with the exact amounts of naltrexone and hydrocodone as listed in claims 2-11 in one composition.

However, it is obvious to vary and/or optimize the amount of hydrocodone and naltrexone provided in the composition, according to the guidance provided by Oshlack et al., to provide a composition having the desired properties such as the desired concentrations of hydrocodone and naltrexone. It is noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). One would be motivated to optimize the

amounts of naltrexone and hydrocodone as taught by Oshlack et al. in order to provide maximal pain relief because Oshlack et al. teach ranges of each drug that overlap with the claimed ranges.

Claims 1-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sherman et al. (US Pg-Pub 2003/0191147) in view of Kaiko et al. (US PgPub 2003/0031712).

Sherman et al. teach compositions comprised of naltrexone hydrochloride in amounts of about 0.1 to less than about 0.5 mg (paragraphs 0058 and 0065). Paragraphs 0062-0063 exemplify the dose amounts of naltrexone contemplated by the invention and conclude to say that any minimum amount and any maximum amount within range of amounts is possible (paragraph 0064). The composition is taught as also having another ingredient in the way of an opioid agonist such as hydrocodone bitartrate (paragraph 0068 and Example 15). Paragraphs 0242-0251 exemplify a study in which the composition of the invention was tested in methods of treating pain. Further controlled release compositions are also contemplated by Sherman et al. (paragraph 0145). Sherman et al. further teaches that in preparing a composition, amounts of naltrexone at 0.1 % and hydrocodone at 10% are added into a mixture before granulation in Example 15, meeting the limitation of the claimed ratio. Sherman further teaches that other active pharmaceutical ingredients such as ibuprofen (paragraph 0069). Sherman teaches oral dosage forms of the compositions

(paragraphs 0070-0071). Sherman teaches the state of the art regarding opioid antagonists being manufactured to prevent abuse of opioid agonists (paragraph 0056).

Sherman et al. does not teach the exact amounts of naltrexone and hydrocodone as listed in claims 2-11 in one composition or that the compositions are interdispersed with a sustained release excipient.

Kaiko et al. teaches formulations comprising hydrocodone and naltrexone (paragraph 0072) can comprise coatings and melt extrusion multiparticulates that aid in releasing the drug over a twelve to twenty-four hour period to provide analgesia (paragraph 0099). Kaiko discusses that opioid antagonists typically block or reverse all of the effects of opioid agonists and that a use of opioid antagonists is as a once-a-day treatment of naltrexone to block the euphoric effects that might otherwise be obtained upon administration of opioids to addicts (paragraph 0011). Kaiko teaches incorporating the opioid agonist and the opioid antagonist into a dosage form that includes a sustained release carrier such that the oral dosage form can be administered on a twice-a-day or once-a-day basis (paragraph 0046).

Furthermore, it is obvious to vary and/or optimize the amount of naltrexone and hydrocodone provided in the composition, according to the guidance provided by Sherman et al., to provide a composition having the desired properties such as the desired concentrations of both drugs in an effort to provide maximal pain relief. It is noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

Accordingly, one of ordinary skill in the art at the time of the invention would have found it obvious to combine the teachings of Sherman et al. which teaches pharmaceutical compositions and methods of making and using such compositions that are comprised of hydrocodone and naltrexone with the teachings of Kaiko et al. which teach similar compositions in which the drugs are interdispersed with sustained release excipients. One would be motivated to do so in an effort to treat pain over a maximal period of time, to increase patient compliance and to reduce the abuse potential of the opioid agonist.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Renee Claytor whose telephone number is (571)272-8394. The examiner can normally be reached on M-F 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Renee Claytor

/SREENI PADMANABHAN/
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